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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/436,164 11/09/99 REUBINOFF

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EXAMINER

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WOITACH, J

ART UNIT

PAPER NUMBER

1632

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/436,164

Applicant(s)

REUBINOFF ET AL.

Examiner

Joseph Weitach

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 1-18 and 29-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 19-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 November 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: 4.

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**DETAILED ACTION**

This application is an original application filed November 9, 1999 which claims benefit of foreign applications PP7009, filed November 9, 1998, and PQ2852, filed September 15, 1999, both filed in Australia.

Claims 1-36 are pending and currently under examination.

***Election/Restriction***

Applicant's election with traverse of groups II, claims 19-28, in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the inventions set forth in the restriction requirement are not independent and distinct. Applicants review the basis of the restriction and argue that the groups I-VII are merely different aspects of the same invention, and are closely related to one another. Further, Applicants argue that classification is an unreliable for the basis of determining independence and distinctness. See Applicants remarks, pages 3-5. Applicants argument have been fully considered but not found persuasive.

Examiner agrees that groups I-VII are related, and as suggested in Applicants arguments regarding the overlap of classification definitions, the search for group I may result in references which may be relevant to groups II-VII. However groups II-VII would require a further search of the art and further considerations. For example, the methods of differentiating an embryonic stem cell, encompassed by group II, can use embryonic stem cells obtained by various means and

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are not limited to the methods of group I. In addition, the inventions of groups III-VII are not necessary for the practice of group II. Furthermore, Examiner agrees with Applicants discussion regarding obvious double patenting, however each of the restricted groups represent inventions that are not obvious one over the other. The methods of differentiation encompassed by group II would not make obvious a means to isolate an embryonic stem cell encompassed by group I. In fact, these are considerably different methods resulting in different products. Additionally, the fibroblast cell lines and various methods of groups III-VII would not make obvious instantly elected invention. Each of the methods and products encompassed by groups I-VII are directed to different inventions and require different method steps to practice and thus, require different searches. For a proper restriction one of two standards must be met: 1) the inventions must be independent or distinct, and 2) there must be a serious burden on the examiner if restriction is not required of a proper restriction has been met (MPEP 806.04 and 808.02). In this case, Applicant does not contest that the inventions are not distinct, only that they are highly related and seem to argue that are not independent because they can be used together. Further, MPEP 808.02 states that 'the Examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation of one of the following: (A) separate classification, (B) separate status in the art when classifiable together, or (C) a different field of search'. In this case, Examiner has demonstrated each A, B and C for the restriction groups.

The requirement is still deemed proper and is therefore made FINAL.

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Claims 1-36 are pending, claims 1-18 and 29-36 are withdrawn from consideration as being drawn to a non-elected invention, and claims 19-28 are currently under examination.

***Priority***

Acknowledgment is made of applicant's claim for foreign priority based on two applications filed in Australia on November 9, 1998, and on September 15, 1999. It is noted, however, that applicant has not filed a certified copy of the applications as required by 35 U.S.C. 119(b).

***Claim Objections***

Claims 19-28 are objected to because of the following informalities: Claims 19-28 are dependent on non-elected claims and inventions. Appropriate correction is required.

Claim 22 is objected to because of the following informalities: 'according' is misspelled. Appropriate correction is required.

***Specification***

The abstract of the disclosure is objected to because it is not present as a single paragraph. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

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The abstract should be in narrative form limited to a single paragraph on a separate sheet within the range of 50 -150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The disclosure is objected to because it contains polynucleotide sequences which are not identified by SEQ ID NOs. Applicants' sequence listing, filed June 29, 2001, paper number 9, has been entered, however the specification has not been amended to clearly indicate the polynucleotide sequence represented by each SEQ ID NO in the sequence listing. Correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of culturing a human pluripotent embryonic stem cell and deriving spontaneously differentiated cell types therefrom, does not reasonably provide enablement for culturing human totipotent embryonic stem cells or methods for the controlled

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differentiation of a stem cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

The basis of the instant rejection focuses on the breadth of the claim and the requirement of the existence of totipotent human embryonic stem cells. The specification does not specifically define an embryonic stem cell however, the present art accepted definition of an embryonic stem cell is a totipotent cell capable of contributing to all tissues of an animal including the germ cells (Nichols *et al.*, page 1341; first paragraph). The specification teaches that human stem cells have been previously described in the art (pages 1-4), and that the instantly claimed methods can be used for isolating and culturing said cells (pages 4-6). It is noted that the specification indicates that embryonic stem cells 'have the capacity to differentiate *in vitro* into a wide array of somatic lineages' (page 9; lines 15-16) and that they are derived from an embryo (page 12; lines 15-21). Further, a review of the entire specification does not indicate that the human embryonic stem cells described in the specification are totipotent and/or capable of contributing to the germ line, however because of the interchanging use of embryonic stem cell and stem cell in the specification, in view of the art accepted definition of an embryonic stem cell, the claims are being interpreted in the greatest reasonable breadth in light of the art accepted definition of a totipotent embryonic stem cell.

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Claims 19-26 are drawn to a method for culturing and differentiating human undifferentiated embryonic stem cells. Claims 27 and 28 are drawn to a differentiated cell derived by said methods. Claims 27 and 28 are included in the rejection because though the claim recites a differentiated cell, the claims clearly intend to encompass a cell with properties associated with a stem cell such as conditions that 'do not permit continued stem cell renewal but do not kill stem cells or induce their unidirectional differentiation' (claim 19) and as 'capable of self renewal' (claim 28), and could reasonably interpreted as a method for and a resulting cell representing a totipotent embryonic cell. The specification states the art teaches that while stem cells from mice and human embryonic carcinoma (EC) cells have been shown to differentiate *in vitro*, differentiation of primate and human stem cells described in the art have been only characterized by expression markers and thus, lack evidentiary data demonstrating that these cells have the capacity to differentiate. It is concluded that the instantly claimed methods represent an invention to overcome or at least alleviate some of the problems of the prior art (page 4; lines 3-15).

The general characteristics attributed to the isolated and cultured stem cells may be reasonably interpreted as totipotent embryonic stem cells. The specification teaches that the primate and human embryonic cells and cell lines were isolated by methods previously described and used for non human primates and teaches that the cell lines are capable of differentiating into cells derived from all the three embryonic germ layers as evidenced by forming teratomas after injection into SCID mice and in vitro analysis of cells grown to confluence. However, there is no

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indication that the cell lines or cells derived from the cell lines are totipotent and capable of contributing to the germ cell.

The state of the art of the claimed invention is not very well established and very few species of animal have had a totipotent embryonic stem cell isolated. Further, the art of isolating embryonic stem cells is highly unpredictable. With regard to a developing embryo, Cruz *et al.* list some of the differences in early embryonic development among swine, oxen, horses, goats and sheep (page 166; Table 1). In addition, Piedrahita *et al.* teach that culturing and isolation conditions for one species may not be suitable for culturing and isolation of embryonic stem-like cells from another species. Specifically, conditions that allowed production of porcine embryonic stem-like cells did not allow development of ovine embryonic stem-like cells (summarized on page 886; Table 1). Therefore, it would be recognized by one of skill in the art that one cannot simply extrapolate from procedures shown effective in one species to use or develop procedures for another species. As taught and demonstrated in Cruz *et al.* and Piedrahita *et al.* numerous attempts to isolate embryonic stem cells from species other than the mouse have been attempted however, demonstration that these cells are able to contribute to the germ line is awaited (summarized by Clark *et al.* page 250; second paragraph).

The specification sets forth procedures for the isolation of primate embryonic stem cells, however, with respect to the human embryonic stem cells isolated by this procedure it has been shown to be successful only as far as the demonstration of certain markers, expression of chorionic gonadotropin and differentiation into cells representative of each of the three

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embryonic germ layers when injected into SCID mice. The specific examples provided in the art by Thomson *et al.* (referenced date of 1995, 1996 and 1998, instant specification page 3) demonstrate that pluripotent rhesus and marmoset embryonic stem cells can be isolated, however, there is no indication that these monkey embryonic stem cells can contribute to the germline, nor is there a nexus between the methods used to isolate the monkey embryonic stem cells and their effectiveness for use in isolating human embryonic stem cells. In the absence of evidence that the methods for the isolation of monkey embryonic stem cells, produce true totipotent embryonic stem cells, the amount of experimentation required to carry out the methods for the isolation of human embryonic stem cells is paramount. Further, the amount of experimentation required to demonstrate that embryonic stem-like cells are true embryonic stem cells is great because the embryonic stem-like cells would require implantation into a blastocyst, growth to term, and demonstration that the mosaicism extends to all tissues including the germ cells.

Finally, the claim methods can reasonably be interpreted as being drawn to methods wherein the differentiating results in a specific somatic cell lineage. The specification contemplates that the methods for differentiation can be used to establish cells of a particular cell type, or to study development and/or tissue regeneration (instant specification, page 25). At the time of filing, the specification suggests that the human embryonic stem cells were not yet shown to be capable of differentiating into somatic cell lineages. Further, the instant specification and the art of record indicates that differentiation of embryonic stem cells into a particular cell type is

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a primarily a random process. That is, though certain culturing conditions are known to result in differentiation, the means to specifically differentiate a stem cell into a particular cell type are not well known. The specification teaches methods in which stem cells are differentiated, however it clearly teaches that after the differentiation a selective cultivation or other means of isolation from the resulting mixed population must be practiced (page 23, lines 10-28). The specification is silent with respect to methods in which only specific types of differentiated cells are generated. Presently, the art recognizes that methods for differentiating embryonic stem cells into specific cell types is still not attainable. As reviewed by Thomson *et al.* (Trends in Biotech, 18:53-57), 'differentiation of ES and EG cells towards specific lineages is currently limited' and 'the resulting population of differentiated cells is always a mixture of different cell types' (page 56, bottom of first column). The only working example presented in the present application indicates that the differentiating culturing conditions taught in the specification also result a mixture of cell types including neurofilaments and muscle, and ultimately embryoid bodies similar to those formed in mouse ES cell aggregates (pages 35-36, bridging paragraph).

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 19-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 19 is vague and confusing because the method is drawn to conditions to 'induce somatic differentiation', however the claim also recites that the stem cells are not killed or are not induced for the 'unidirectional differentiation into extraembryonic lineages'. It is unclear how differentiation can occur if the stem cells cannot or culturing conditions do not permit the differentiation of the stem cell. Further, the claim is unclear in the recitation of 'unidirectional' because it is unclear if the claim intends to encompass conditions culturing cells wherein the resulting differentiated cell is capable of de-differentiating back into a stem cell. The specification provides no support for this property of the cultured cell, and in view of the instant specification and the art of record, it is unclear if a differentiated cell is even capable of returning to the state of pluripotency once it has committed to a particular lineage. Further, dependent claims 20-28 are included in this rejection because they fail to clarify the basis of the rejection.

Claim 20 is vague and unclear in the recitation of 'a differentiated somatic lineage or multiple somatic lineage' because it is unclear if the same culturing condition is responsible for both a single lineage and multiple lineages. It is unclear if the method results in two separate outcomes because of the stem cell used or because of some culturing step which controls the deaferentiation into a particular lineage. Either, the claimed method seems to lack essential steps

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which would provide the means to produce a single lineage or multiple lineages, or the instantly claimed method inherently results in both possibilities regardless of the conditions used and should recite --a somatic lineage and multiple lineages--.

Claims 20-25 are vague and confusing in the recitation of 'a differentiation inducing fibroblast feeder layer' because the specification describes the fibroblast feeder layer as necessary for the maintenance of the pluripotency of the stem cells (pages 15-16, starting on line 13), and it is only the culturing conditions on the feeder layers, not the feeder cells themselves, which results in the differentiation of the stem cell. It is unclear if Applicants intend to use a fibroblast cell which is not described in the instant specification or the claim means to refer to the culturing conditions in the presence of fibroblast feeder cells.

Claim 23 is unclear and confusing because the method of claim 19 is drawn to a method of somatic differentiation, however claim 23 recites a test for fibroblast feeder cells which limit extraembryonic differentiation. The nexus between practicing the elected methods of differentiation and the method of claim 23 is not clear, and would not result in the intended outcome set forth in the preamble of claim 19.

Claim 26 is vague and unclear because the methods of claims 19-25 should result in differentiated somatic cells as recited in the preamble of claim 19, however claim 26 recites that 'progenitor cells' are isolated. It seems that practicing the methods recited in claims 19-25 also results in the formation of progenitor cells, however there is insufficient antecedent basis for 'a committed progenitor cell' in any of the preceding claims. Further, even if both cell types are

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generated, somatic and progenitor cells, in light of the teachings of the instant specification it is unclear how the artisan would differentiate and thus isolate a committed progenitor cell from a non-committed progenitor cell, or from the cell population in general.

Claims 27 and 28 are vague and unclear, because as noted above for claim 19, the differentiated cell seems to encompass properties of the undifferentiated stem cell, and it is unclear if this is an inherent property of some type of somatic cell present in the culture or is in reference to stem cells which do not somehow fully differentiate. If the cell is not fully differentiated, would it still be considered a differentiated somatic cell?

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 19-28 are rejected under 35 U.S.C. 102(b) as being anticipate by Thomson *et al.* (Science 282:1145-1147).

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Claims 19-26 are drawn to a method for culturing and differentiating human undifferentiated embryonic stem cells. Claims 27 and 28 are drawn to a differentiated cell derived by said methods. Note, in view of the 35 USC 112, second paragraph, rejection over the nature of the differentiated cell, claims 27 and 28 are being interpreted as a cell with properties associated with a stem cell such as conditions that 'do not permit continued stem cell renewal but do not kill stem cells or induce their unidirectional differentiation' (claim 19) and as 'capable of self renewal' (claim 28), and could reasonably interpreted as an embryonic cell, or alternatively as a fully differentiated cell. Further, regarding the differentiated cells, it should be noted that patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claims. *In re Thorpe*, 227 USPQ 964 (Fed. Cir. 1985). In the instant case, because of the breadth of the claim and the fact that similar types of differentiated cells can be obtained by various methods, the recitation that the differentiated somatic cell be obtained from a specific method is not sufficient to differentiate the instantly claimed culture from any other somatic cell. Further, where, as here, the claimed and prior art products are identical or substantially identical, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. *In re Ludtke*. Whether the rejection is based on "inherency" under 35 USC 102, on "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re*

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*Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Thomson *et al.* teach human pluripotent embryonic cell lines. Specifically, Thomson *et al.* teach three cell lines: H13 and H14 which have a normal XY karyotype and H7 which has a normal XX karyotype (page 1145; second column). Thomson *et al.* teach that when the cell lines are injected into an immunodeficient mouse the cell lines can differentiate into endoderm, mesoderm and ectoderm cell types (page 1146; middle of first column and page 1147; figure 4). Further, characterization of the lines in culture, differentiation of the cells results in various cell types, including neuronal cells (neural epithelium shown in figure 4B). Thus, the differentiated cells which developed from pluripotent embryonic cells taught in Thomson *et al.* anticipate the differentiated cells in claims 27 and 28. In addition, in characterizing the cell lines, various culturing methods were used to differentiate the cell lines. Among the parameters taught to affect differentiation of the cell lines was the feeder layer, the cell density, and various growth factors. In view of the breadth and generality of the claimed methodology in claims 19-26, the methods and general teachings of Thomson *et al.* describing methods to stimulate or allowing the cell lines to differentiate in culture, anticipate the methods of claims 19-26.

Claims 19-28 are rejected under 35 U.S.C. 102(e) as being anticipate by Thomson (US Patent 6,200,806).

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Claims 19-28 are summarized above. As reasoned above, any cell differentiated into a human somatic cell and any human differentiated cells would anticipate the instant claims. Thomson teaches a purified preparation of pluripotent human embryonic stem cells which are capable of differentiating into derivatives of the endoderm, mesoderm and ectoderm (specifically encompassed by claim 1). In the characterization of the cells it is demonstrated that the cells can differentiate into neural cells (column 11; lines 31-32). Further, conditions to culture the cells in gelatin treated culture plates is taught when placed in culture and allowed to grow for two weeks after achieving confluence, or grown without a fibroblast feeder layer the cells spontaneously differentiate (description in paragraphs bridging columns 14-15 and in Figure 6). Thus, the differentiated human cells and methods to differentiate said cells from pluripotent embryonic cells taught in Thomson *et al.* anticipate the claims.

Claims 27 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Kaufman *et al.* (US Patent 6,280,718).

Claims 27 and 28 are summarized above. As summarized above, any human differentiated would anticipate the primate/human cell encompassed by claims 27 and 28. Kaufman *et al.* teach a method of obtaining human hematopoietic cells from human pluripotent embryonic cells (method set forth in claim 1). The embryonic cells after being cultured in conditions for differentiation produced CD34+ cells with a cobblestone morphology (column 7;

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lines 29-32). Thus, the differentiated human cells which developed from pluripotent embryonic cells taught in Kaufman *et al.* anticipate the claims.

Claims 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Damjanov *et al.* (Lab. Invest. 68:220-232)

Damjanov *et al.* teach the human germ cell line NCCIT, and in the characterization of the NCCIT cell line Damjanov *et al.* demonstrate that the cell line can differentiate into all three embryonic germ layers, ectoderm, mesoderm and endoderm (summarized on page 220, abstract and detailed section on immunochemistry pages 222-224). While the differentiated cells disclosed in Damjanov *et al.* are not specifically derived from the cell lines disclosed in the instant application, or a embryonic stem cell, a differentiated human cell as claimed would be indistinguishable from those disclosed in Damjanov *et al.* Patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claims. *In re Thorpe*, 227 USPQ 964 (Fed. Cir. 1985).

The post filing art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ororico *et al.*, Stem Cells 19:193-204, 2001. Discloses that the human embryonic stem cell lines previously taught in Thomson *et al.* (Science, 282:1145-1147, the references used in the 35 USC

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102(b) rejection above), are capable of fully differentiating in culture under conditions previously described.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached at (703)305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Kay Pinkney whose telephone number is (703)306-3076.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

  
DEBORAH CROUCH  
PRIMARY EXAMINER  
GROUP 1630